Rec'd PCT/PTO 24 JUN 2005

/540766

(12) INTERNATIONAL [illegible]LICATION PUBLISHED UNDER THE PATEN[illegible]OPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
15 July 2004 (15.07.2004)

PCT

(10) International Publication Number
WO 2004/058056 A1

(51) International Patent Classification⁷: A61B 3/11

(21) International Application Number: PCT/GB2003/005653

(22) International Filing Date: 23 December 2003 (23.12.2003)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0230223.0 24 December 2002 (24.12.2002) GB

(71) Applicant *(for all designated States except US)*: **NEWCASTLE-UPON-TYNE HOSPITALS NHS TRUST** [GB/GB]; Freeman Hospital, High Heaton, Newcastle-upon-Tyne NE7 7DN (GB).

(72) Inventors; and

(75) Inventors/Applicants *(for US only)*: **CLARK, Andrew** [GB/GB]; 27 Byron Avenue, Boldon Colliery, Tyne & Wear NE35 9DT (GB). **CHAMBERS, Iain, R.** [GB/GB]; 20 Ripley Drive, Cramlington, Northumberland NE23 7XA (GB).

(74) Agent: **ELSWORTH, Dominic, Stephen**; Hargreaves Elsworth, Rotterdam House, 116 Quayside, Newcastle-upon-Tyne NE1 3DY (GB).

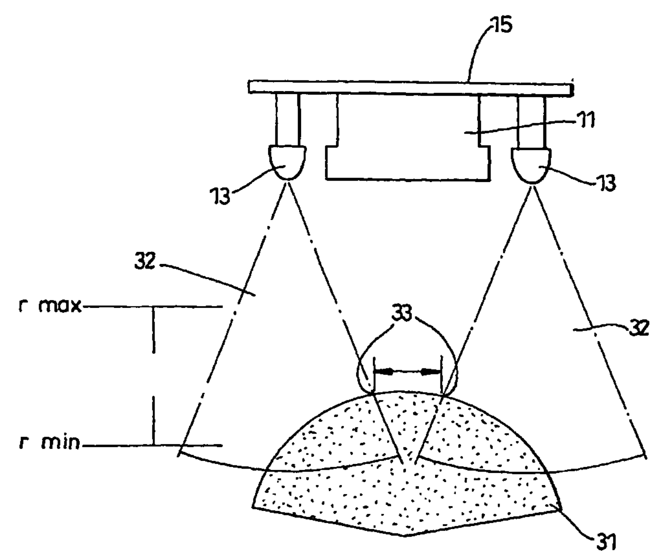
(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*

[Continued on next page]

(54) **Title:** A PUPILOMETER



(57) **Abstract:** A pupilometer comprises image capturing means, illumination means comprising two spaced apart light sources, stimulation means, and image processing software, the illumination means generating and emitting light of a first wave-length, and the stimulation means generating and emitting light of a second wavelength. The illumination means is arranged to one or both sides of said image capturing means and, in use, shines light towards the eyeball, the image processing software receiving data from the image capturing means, and by processing said data according to an algorithm establishes the distance between the surface of the eyeball and the camera.

WO 2004/058056 A1

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

A Pupilometer

Field of the Invention

This invention relates to an apparatus commonly known as a pupilometer.

Background of the Invention

In the neurological assessment of an unconscious patient, pupil response is known to be a vital aspect of the diagnostic process. Regular assessment of the size, reactivity to light and equality of pupils is essential for early recognition of neurological deterioration in situations where intra-cranial pathology is a threat. As such this assessment is regularly carried out in paramedic, intensive and high dependency care situations.

The current method of practice is to manually measure these aspects using a bright light, which stimulates reactivity of the pupil, and make a note of the dilation compared to the original size of the pupil. Actual measurements taken are then compared with a card having different pupil sizes marked thereon. This method of assessment is time consuming, and subjective.

Pupilometers have been developed for use in the assessment of eye shape and condition, monitoring tiredness, and in the detection of drugs or alcohol in a person.

A hand-held pupilometer is described in US 6,022,109 (Dal Sante). This pupilometer detects and measures pupil diameter and pupil response to a light stimulus. Also described is software to permit the diagnosis of alcohol or drug presence. However, use of this pupilometer requires the active participation of the user.

Another hand-held pupilometer is described in US 6,199,985 (Anderson). This patent describes a method for measuring optical power output from the pupil. However, the pupilometer described in the patent requires complex optometric components.

Another hand-held pupilometer is described in US 6,260,968 (Stark). The device described includes an LCD display via which prompts to the operator are given. The pupilometer described in this patent uses a "flying spot" algorithm to establish a circumference fitting the pupil, and the pupil radius. The pupilometer includes software to aid diagnosis. Again, the pupilometer described in this patent requires complex optometric components.

It would therefore be desirable to provide an improved pupilometer.

Summary of the Invention

According to one aspect of the invention there is provided a pupilometer as specified in Claim 1.

According to another aspect of the invention, there is provided image processing software as specified in Claim 34.

The software may be embodied on a record medium, stored in a computer memory, embodied in read only memory, or carried on an electrical signal.

According to another aspect of the invention, there is provided a process for obtaining pupil image information as specified in Claim 35.

According to another aspect of the invention, there is provided a hand-held pupilometer as specified in Claim 36.

Brief Description of the Drawings

In the drawings, which illustrate exemplary embodiments of pupilometers according to the invention:

Figure 1 is a schematic representation of a perfect eye;

Figure 2 is a block diagram of a pupilometer;

Figure 3 is a schematic representation of an eyeball;

Figure 4 is an image of an eye under ambient light;

Figure 5 is an image of an eye under infra-red light;

Figure 6 shows a raw image taken by the pupilometer before any image processing has taken place;

Figure 7 shows the image of Figure 6 after the identification of dark pixels;

Figure 8 is a table used to identify an edge;

Figure 9 shows the image of Figure 7 after identification of the pupil edge;

Figure 10 shows the image of Figure 9 at the beginning of a spiral search;

Figure 11 shows the image of Figure 9 with adjoining pupil edge pixels connected to one another;

Figure 12 is a table illustrating a recursive flood-fill algorithm;

Figure 13 shows the image of Figure 11 with the rectangular dimension of the pupil identified;

Figure 14 shows an image of a part of an eye close to the pupil when subjected to highlights from infra-red LED's of the pupilometer;

Figure 15 shows the image of Figure 14 with possible highlights marked;

Figure 16 shows the comparison of highlight vertical co-ordinates in Figure 15;

Figure 17 shows identification of the highlights of Figure 16 with the closest vertical alignment;

Figure 18 shows the image of Figure 17 with the distance between the two valid highlights marked;

Figure 19 is a graph showing the reaction over time of a pupil diameter to a light stimulation;

Figure 20 is a schematic cross-section of a hand-held pupilometer;

Figure 21 is a plan view of the pupilometer illustrated in Figure 20;

Figure 22 is a block diagram of the pupilometer shown in Figures 20 and 21;

Figure 23 is a schematic representation of a pupilometer of the invention in close proximity to an eye; and

Figure 24 shows an image of a part of an eye close to the pupil when subjected to highlights from infra-red LED's of the pupilometer;

Figure 25 shows the image of Figure 14 with the highlights marked;

Figure 26 is a schematic representation of the marked highlights of Figure 15;

Figure 27 shows the image of Figure 14 with the distance from the highlight to the centre marked; and

Figure 28 shows the image of Figure 14 with the distance between the two highlights marked.

Detailed Description of the Preferred Embodiments

Figure 2 illustrates the components of an embodiment of the pupilometer. The pupilometer comprises a camera board 10 including a camera, which in the example is a CMOS (Complementary Metal Oxide Semiconductor) camera 11, a filter 12, which in the example is an infra-red pass filter, a pair of infra-red light emitting diodes (IR LED's) 13, and a light emitting diode (LED) 14 for emitting white light. The camera 11 and LED's 13, 14 are mounted on a board, which in the example is a printed circuit board 15, the filter 12 being mounted in front of the lens of the camera 11.

The camera board 10 is connected by suitable cabling to a control board 20, which mounts an analogue interface 21, a micro-controller 22, a memory 23 and a Universal Serial Bus (USB) interface 24. The analogue interface 21, memory 23 and USB interface 24 are each connected to the micro-controller 22 by suitable cabling 25. The analogue interface 21 receives an analogue video signal from the camera board 10 and converts said signal into a digital form. The micro-controller 22 provides control signals for image acquisition from the camera board 10, and transmission of image data to a computer programmed with custom pupil detection and measurement software, which in the example is a laptop computer 26 connected to the micro-controller 22 via a USB interface 24. However, the computer programmed with custom pupil detection and measurement software could easily form part of a hand held pupilometer device. Such a device is described with reference to Figures 20 to 22.

The control board 20 also mounts a memory module 23 which provides additional static RAM for storage of image data acquired from the camera board 10 prior to transmission of the image data to the computer 26, with the USB interface 24 providing a physical interface for the conversion and transmission of image frames to the computer 26 over a standard USB interface.

The computer 26 of the example runs the operating system, "Microsoft Windows 95", and custom software which detects and measures the pupil in the images generated by the camera.

Referring now to Figure 3, the IR LED's 13 shine light towards the eyeball 30, but to the sides of the pupil 31. By virtue of illuminating the eyeball by shining light to the sides of the pupil 31, most of the rays of light entering the pupil are internally reflected and absorbed by the retina, and thus the camera only sees light reflected from the surface of the eye, with the pupil appearing as a dark area.

The purpose of the infra-red pass filter 12 is to stop all visible light entering the camera 11, which eliminates the effects of ambient light conditions, thereby permitting accurate control of the instrument.

Figures 4 and 5 illustrate the difference in appearance of an eye under ambient light conditions (see Figure 4) and infra red lights (see Figure 5). In Figure 5, the contrast between the pupil 3 and the iris 2 is increased compared to Figure 4. Also, there is much less surrounding detail in Figure 5 compared to Figure 4.

The reflections from the IR LED's 13 can be seen clearly in Figure 5, and the distance between these specular highlights is used as measure of the distance from the camera to the eye (the closer the IR LED's are to the eye, the further apart are the highlights).

Referring now to Figure 23, the eye 1 is illuminated by light in the infra-red spectrum of light beams 32 emitted by the infra-red LED's 13. The camera 11 sees highlights 33 on the surface of eyeball 30. For the pupilometer to generate an output of pupil size, separate highlights from each infra-red LED 13 must be detectable, and therefore must be within a certain distance of the surface of the eyeball. The extremes of the light beams 32 are illustrated by dotted lines. Clearly, if the infra-red LED's are too far away from the surface of the eyeball, they will overlap, in which case two spaced apart highlights 33 would not be appear on the surface of the eyeball. Conversely, if the infra-red LED's are too close to the surface of the eyeball, then the highlights will be so far apart as to be located in close proximity to the eyelids, rather than in the central region of the surface of the eyeball 30. In such a situation, the two highlights cannot be detected. Therefore, if the pupilometer is outside the range r_{min}-r_{max}, where r_{min} is the minimum distance from the infra-red LED's to the surface of the eyeball 30, and r_{max} is the maximum distance of the infra-red LED's to the surface of the eyeball 30, two separate highlights cannot be detected, and the pupilometer software produces a range error signal. The algorithm restarts the ranging step after pupil detection in the next captured image.

Referring now to Figures 20 to 22, there is shown a hand-held pupilometer, which comprises a camera board 110 including a camera, which in the example is a CMOS (Complementary Metal Oxide Semiconductor) camera 111, a filter 112, which in the example is an infra-red pass filter, a pair of infra-red light emitting diodes (IR LED's) 113, and a light emitting diode (LED) 114 for emitting white light. The camera 111 and LED's 113, 114 are mounted on a board, which in the example is a printed circuit board 115, the filter 112 being mounted in front of the lens of the camera 111.

The camera board 110 is connected to a control board 120, which mounts an analogue interface 121, a micro-controller 122, a memory 123 and a computer interface 106. The analogue interface 121, memory 123 and computer interface 106 are each connected to the micro-controller 122 by suitable cabling 125. The analogue interface 121 receives an analogue video signal from the camera board 110 and converts said signal into a digital form. The micro-controller 122 provides control signals for image acquisition from the camera board 110. Further, the micro-controller 122 transmits image data to, and runs, custom pupil detection and measurement software.

As mentioned above, the control board 120 also mounts a memory module 123 which provides additional static RAM for storage of image data acquired from the camera board 110 for use by the custom pupil detection and measurement software of the micro-controller.

The computer interface 106 provides a physical interface for transmission of data to an external computer. It may be desirable to store test results in patients' notes, or for research purposes, and whilst the hand-held device 100 has sufficient memory to record a number of results, to use the device continually, the memory 123 must be cleared from time to time.

As with the device described with reference to Figure 3, the IR LED's 113 shine light towards the eyeball 30, but to the sides of the pupil 31. By virtue of illuminating the eyeball by shining light to the sides of the pupil 31, most of the rays of light entering the pupil are internally reflected and absorbed by the retina, and thus the camera only sees light reflected from the surface of the eye, with the pupil appearing as a dark area.

Pupilometer Software

The main function of the software is to interpret the image of the eye and detect, or classify, the pupil within that image. The software was developed using Borland Delphi and in the example executes under the Microsoft Windows operating system.

The basic requirement is the ability to detect a circle (i.e. the pupil) within the image and known algorithms available for the performance of this task include the Hough transform, parametric matching and neural network classification. However, these methods are computationally intensive and require a floating-point numeric processor in order to achieve optimal performance.

One aim of the invention to provide a standalone hand-held pupilometer. This means that a relatively low specification microprocessor must be used and therefore the algorithm of the invention is a simple multi-stage classification algorithm, which uses integer mathematical functions to classify the pupil within the image.

Referring now to Figure 1, there is shown a model of a perfect eye, i.e. the iris 2 is at the centre of the eyeball 1, with the pupil 3 being at the centre of the iris 2. Further, both the pupil 3 and the iris 2 are perfect circles, the boundary 4 between the iris 2 and the pupil 3 is sharp, and the darkest region of the eye is the pupil 3.

The software of the invention makes certain assumptions based on the model of the perfect eye described above, those assumptions being:

1) The pupil will be the darkest area of the image;

2) The pupil – iris boundary will have the sharpest edge;

3) The pupil – iris boundary will be elliptical.

The software provides three principal functions;

1. *Pupil classification:* the detection and measurement of the pupil within the image of the eye.

2. *Ranging:* the detection and measurement of the IR LED reflections on the eye surface allowing calculation of distance from camera to eye.

3. *Stimulation:* measurement of the pupil reflex action to light stimulation.

Pupil Classification

The classification algorithm of the invention provides for the differentiation of the pupil from other dark areas of the image, such as shadows, and from interference within the pupil boundary, for example eyelashes and highlights.

The control board 20 transmits a new image every 200ms via the USB interface 24. The image is returned as a two-dimensional (128 x 128 pixel) array of 6 bit values, with each value representing the greyscale intensity of the relevant image pixel in the range 0 to 63. This image is then subjected to the following processing steps:

1) As the raw image array is read into the Delphi program, the values of the darkest (**Vdark**) and the lightest (**Vlight**) pixels are calculated and stored. Threshold levels are then calculated using these values; **Tdark=Vdark+4** and **Tlight=Vlight-2** – see Figure 6.

2) All image pixels with values of less than or equal to this dark threshold (**Td**) are assigned to the ***PUPIL*** class – see Figure 7.

3) The edge values across each of these ***PUPIL*** class pixels are calculated using the simple gradient algorithm **|P4-P0| +|P4-P1| +|P4-P2| +|P4-P5| +|P4-**

P8| +|P4-P7| +|P4-P6| +|P4-P3| =G the gross radial gradient. This algorithm produces the gross radial gradient (G) across the central pixel (P4) – see Figure 8.

4) All image pixels with edge values (G) of greater than or equal to 8 are assigned to the *PUPIL_EDGE* class - see Figure 9. The pupil edge value of 8 was selected using empirical methods as a value discriminating valid edge pixels.

5) In order to locate an area of *PUPIL_EDGE* pixels large enough to be the actual pupil, a spiral search is initiated from the centre of the image (or the centre of a valid pupil from the previous frame to improve the speed of location), is used to locate the first *PUPIL_EDGE* pixel and this is assumed to lie on the pupil boundary – see Figure 10.

6) When the search locates a *PUPIL_EDGE* pixel – see Figure 10, All adjoining *PUPIL_EDGE* pixels are connected using a recursive flood fill algorithm. The fill algorithm also tracks the numbers and extents of the adjoining pixels, from which the width and height of pupil region are derived – see Figure 11. If the fill connects more than 16 pixels, the area is designated as being the **pupil boundary area** and the algorithm continues to step 7. If the fill connects less than 16 pixels, the area is designated as being too small to be the pupil and the spiral search (5) continues outwards until another **PUPIL EDGE** region is found or the extents of the image are reached. If the pupil boundary area has not been located by the end of the spiral search, the algorithm restarts at step 1 with the next captured image.

In steps 5 and 6, every time the spiral search hits a PUPIL_EDGE the region is flood filled to try to find a region large enough to be the pupil. When the pupil is identified, the spiral search exits.

Recursive flood fill

The fill algorithm sets the target pixel and tests each of its four neighbours, in north-west-south-east order, for another ***PUPIL EDGE*** pixel. As soon as such a pixel is found, the algorithm re-calls itself with this new pixel as its target. An enlarged view of a typical fill pattern is shown in Figure 12. The first branch is filled by the routine calling itself nine times and stops when no further ***PUPIL EDGE*** pixels are found, the second branch (dotted arrows) search then starts. In this way, the routine continues until all adjoining ***PUPIL EDGE*** pixels have been set – see Figure 12.

The rectangular dimension of the pupil boundary area is calculated from the extents of the flood fill and an ellipse consisting of thirty-two points is fitted inside this rectangle. If twelve or more of these points hit a ***PUPIL EDGE*** pixel the region is classified as the ***PUPIL*** and the range detection phase begins; if not the search re-starts with the next captured image. The pupil diameter is defined as the maximum diameter of the ellipse – see Figure 13.

Ranging

When a valid pupil has been classified it is known that the highlights from the infra red LED's will appear in the image within close proximity to the pupil. Therefore to improve speed of calculation and removal of artefacts from eyelids etc, only the area around the pupil is searched.

A first procedure for ranging is illustrated in Figures 14 to 18, and is described below. The search identifies discrete groups of pixels which could belong to valid highlights

With reference to Figure 14, a search area 84 wide by 64 pixels high centred around the pupil is scanned to identify pixels with values of greater than or equal to the previously assigned threshold **Tlight**, these are classed as **HIGHLIGHT_TEST** pixels. When such a pixel is found, a flood fill of adjoining **HIGHLIGHT_TEST** pixels is initiated during which the number of pixels and centre co-ordinates of the fill area is recorded.

Possible highlights are defined as fill areas with pixel counts within the range 4 to 256 pixels, and figure 15 illustrates the identification of such areas. These areas are designated as possible valid highlights and their centre co-ordinates and pixel counts are stored in an array. In order to minimise memory usage, a maximum of 16 areas are allowed.

As shown in Figure 16, when the whole search area has been scanned and two or more possible highlight areas identified, the vertical positions of all areas are compared in order to identify the two areas with the closest vertical alignment.

Figure 17 shows the identification of two such areas.

If less than two or no suitably aligned highlights have been identified, the algorithm is unable to derive range information, and a "range error" signal is generated and the pupil detection phase restarts on the next captured image.

Figure 18 illustrates the final range step, where with both valid highlight areas identified, the horizontal distance between their centres and the geometry of the infra-red LED position and the light emitted thereby allow the software to calculate accurately the distance of the pupilometer from the surface of the patients eyeball. If the distance to

the eyeball is outside the valid detection range r_{min} to r_{max}, the algorithm will generate a "range error" signal and the pupil detection phase restarts on the next captured image.

A second procedure for ranging is illustrated in Figures 24 to 28 is described below.

With reference to Figure 24, an area twelve pixels above and below the pupil is scanned to find the *BRIGHTEST* pixel level.

With reference to Figure 25, the area is rescanned and pixels with a value greater than *BRIGHTEST-8* are marked as *HIGHLIGHT* pixels. The maximum x/y extent of these *HIGHLIGHT* pixels is recorded and the **centre** of the **extents** is calculated.

Centre X = (Max Highlight X – Min Highlight X) / 2

Centre Y = (Max Highlight Y – Min Highlight Y) / 2

Figure 26 illustrates horizontal lines of pixels, starting from the centre pixel (**PASS 1**) and expanding one pixel vertically above and below the centre line (**PASS 2…**), which are scanned to the right hand extents until a HIGHLIGHT pixel is found.

Figure 27 shows the HIGHLIGHT area flood-filled, with the centre of the area calculated from the extents of the flood-fill. Steps 16 and 17 are then repeated for the pixels on the left-hand side of the centre pixel.

Figure 28 illustrates the next step, where with both highlight areas identified, the horizontal distance between their centres is used as a measure of the range.

Stimulation

A lookup table is used to calculate the absolute pupil diameter in millimetres from the measures of pupil pixel diameter and range. When a valid pupil measurement has been

made, the system can start a stimulation cycle to obtain the pupil constriction response curve after stimulus by a bright white light source. The LED 14 generates white light. In a stimulation cycle the LED 14 is energised. In this example, the period during which the LED 14 is energised for approximately 600 ms.

During the stimulation cycle, the pupil diameter is continuously measured and recorded using the above described algorithm whilst the white LED is energised. A graph, illustrated in Figure 19, of the pupil diameter is then drawn, a typical response curve is shown below.

Where the following measurements can be taken;

L	Latency (ms)	Time between start of stimulus and beginning of contraction
A	Contraction amplitude (mm)	Difference between the mean post-stimulus diameter and minimum per-stimulus diameter
Tc	Contraction time (ms)	Time from end of latency to minimum pupil diameter

In the case of a hand-held pupilometer as described with reference to Figures 20 to 22, the graph may be displayed on the display 102 of the hand-held device, or on a VDU.

The response curve can be used in itself in diagnosis, or the response curve can form part of an expert system, which may generate a diagnosis.

The invention allows for the calculation of the distance between the surface of the eyeball and the camera. No spacer of fixed dimension is required to establish a pre-determined distance between the camera and the surface of the eyeball.

Furthermore, there is no requirement for a patient being examined to keep its head still, and look in a fixed direction. The pupil of the patient being examined need not be

aligned with the centre of the camera. The pupilometer of the invention functions as long as the infra-red LED's produce highlights in the vicinity of the pupil. As well as permitting examination of semi-conscious or unconscious patients, the pupilometer can be used on patients who cannot necessarily follow instructions, for example children, impaired individuals, animals, etc. Rather than assuming that the pupil is a dark area in the centre of the image, the pupil finds the dark pupil anywhere in the image.

The invention provides a simple and relatively low cost device for use in a variety of operational situations. Further, it provides a reliable and objective means of assessing pupil response.

Claims

1. A pupilometer comprising image capturing means, illumination means comprising two spaced apart light sources, stimulation means, and image processing software, wherein said illumination means generates and emits light of a first wave-length, and said stimulation means generates and emits light of a second wavelength, and wherein said illumination means is arranged to one or both sides of said image capturing means and, in use, shines light towards the eyeball, wherein the said image processing software receives data from the image capturing means, and by processing said data according to an algorithm establishes the distance between the surface of the eyeball and the camera.

2. A pupilometer according to Claim 1, wherein the step of establishing the distance between the surface of the eyeball and the camera includes finding highlights on the surface of the eyeball generated by the said illumination means and calculating the distance between said highlights.

3. A pupilometer according to Claim 1 or 2, wherein the wavelength of the light generated by said illumination means is in the infra-red spectrum.

4. A pupilometer according to Claim 3, wherein each light source is an infra-red light emitting diode.

5. A pupilometer according to any preceding claim, wherein the image capturing means has an optical axis, and wherein the said two spaced apart light sources shine light in a direction substantially parallel to the optical axis of the said image capturing means.

6. A pupilometer according to any preceding claim, wherein said stimulation means comprises a light emitting diode generating and emitting light in the visible spectrum.

7. A pupilometer according to any preceding claim, wherein said image capturing means comprises a camera.

8. A pupilometer according to any preceding claim, further comprising an optical filter mounted on the [camera] <u>image capturing</u> means.

9. A pupilometer according to Claim 8, wherein the optical filter passes only light of the said first-wavelength.

10. A pupilometer according to Claim 7 to 9, wherein said camera generates a video signal.

11. A pupilometer according to any of Claims 7 to 10, wherein said camera is a complementary metal oxide semiconductor device.

12. A pupilometer according to any preceding claim, wherein said image detection means further includes a micro-controller including a micro-processor.

13. A pupilometer according to any preceding claim, further comprising an analogue to digital converter arranged between said camera and said micro-controller.

14. A pupilometer according to any preceding claim, further comprising memory means.

15. A pupilometer according to any preceding claim, further comprising data input means and display means.

16. A pupilometer according to any preceding claim, further comprising an interface for linking said pupilometer to an external computer.

17. A pupilometer according to any preceding claim, wherein said pupilometer is a hand-held device, wherein said hand held device mounts, said image capturing means, illumination means, stimulation means, image processing software, data input means, display means, a computer interface, said hand-held device including a hand grip.

18. A pupilometer according to Claim 18, wherein, in use the user views the image of the eye displayed on the display means, the said image having been captured by said capture means and processed by said image processing software.

19. A pupilometer according to Claim 15 or 16, further comprising a power supply consisting of a battery.

20. A pupilometer according to any preceding claim, wherein said image processing software includes an algorithm, wherein said algorithm:

i) commands the illuminating means to illuminate an eye;

ii) detects the pupil within the image of the eye;

iii) measures the size of the detected pupil;

iv) establishes the distance of the from the camera to the eye;

v) stimulates a pupil reflex action; and

vi) measures the pupil reflex action.

21. A pupilometer according to Claim 20, wherein the step of detecting the pupil within the image of the eye consists of acquiring image data in the form of a two-dimensional array of values, each value representing the greyscale intensity of an image pixel, and processing said image data according to the following sub-steps:

i) Read the image data into a program;

ii) Run the program to identify the darkest pixel;

iii) Calculate a threshold value as a function of the darkness of the darkest pixel;

iv) Identify and store all pixels as dark or darker than the threshold value as of the pupil class;

v) Calculate the edge value across each pixel in the pupil class;

vi) Establish an edge value threshold value, wherein all image pixels with an edge value greater than or equal to the threshold are identified and stored as pupil edge class;

vii) Execute a search of the image to locate the first pixel in the pupil edge class and assume that this pixel lies on the pupil boundary;

viii) Run an algorithm to connect adjoining pupil edge pixels;

ix) Calculate the rectangular dimension of the pupil region, and fit an ellipse consisting of n points inside the rectangle;

x) If more than n/c (where c is a nominal value) of said n points coincide with a pupil edge pixel classify the region as the pupil and if less than n/c re-start the search with a new image; and

xi) Record pupil radius as the maximum radius of the ellipse.

22. A pupilometer according to Claim 21, wherein said program is a Delphi program.

23. A pupilometer according to Claim 21 or 22, wherein the said edge value is calculated according to a gradient algorithm, wherein the gradient algorithm provides that the gross radial gradient (G) across a central pixel P_4 in an eight pixel array equals $|P4-P0|+|P4-P1|+|P4-P2|+|P4-P5|+|P4-P8|+|P4-P7|+|P4-P6|+|P4-P3|=G$, and wherein the edge value threshold is a function of G the gross radial gradient.

24. A pupilometer according to any of Claims 21 to 23, wherein said search of the image to locate the first pixel in the pupil edge class is a spiral search from the centre of the image.

25. A pupilometer according to any of Claims 21 to 24, wherein said algorithm is a recursive flood fill algorithm.

26. A pupilometer according to any of Claims 21 to 25, wherein n equals 32.

27. A pupilometer according to any of Claims 21 to 26, wherein c equals 2.

28. A pupilometer according to any of Claims 21 to 27, wherein the step of establishing the distance of the pupilometer from the eye includes identifying highlights resulting from the illumination means by the following steps:

i) scan the image for the brightest pixel;

ii) re-scan the image and mark those pixels with a value greater than the brightest eight as highlight pixels;

iii) Record the extents of the highlight pixels in the x and y directions;

iv) Calculate the centre of the extents;

v) Perform a search of the highlight extents until a highlight pixel is found;

vi) Flood-fill the area around the highlight pixel and calculate the centre of the fill area.

vii) Repeat steps v and vi for the other side of the highlight extents

viii) Calculate the horizontal distance between the centres of the highlight areas and store said value as a range value.

29. A pupilometer according to Claim 28, wherein the said search of the highlight extents consists the following step:

i) Perform from the centre of the extents a multi-pass expanding search of one side of the highlight extents until a highlight pixel is found.

30. A pupilometer according to any of Claims 21 to 27, wherein the step of establishing the distance of the pupilometer from the eye includes identifying highlights resulting from the illumination means by the following steps:

i) scan pixels centred around the pupil for pixels with a brightness value greater than a threshold value;

ii) classify all pixels with a brightness value greater than the threshold as Highlight_Test pixels;

iii) flood fill pixels adjoining the Highlight_Test pixels and record number of pixels and the co-ordinates of the fill area;

iv) designate the areas from step iii as possible highlights;

v) compare the vertical positions of all possible identified highlight areas and identify the two highlight areas having the closest vertical alignment;

vi) compare the number of pixels in the two highlight areas having the closest vertical alignment, and the number of pixels spacing the highlight areas aligned vertically most closely;

vii) if the difference in the number of pixels in the two highlight areas having the closest vertical alignment is not greater than a threshold value, and the number of pixels vertically spacing the two highlight areas is not greater than another threshold value, classify the two highlight areas as highlights;

viii) calculate the horizontal distance between the centres of the highlight areas and store said value as a range value.

31. A pupilometer according to any preceding claim, wherein stimulation of a pupil reflex reaction comprises the following steps:

i) establish absolute pupil diameter using the measures of pupil diameter and range;

ii) commence a stimulation cycle by stimulating the pupil with a bright light source for a time period;

iii) record a pupil constriction response curve during and after said stimulus;

iv) display pupil constriction response curve on said display.

32. A pupilometer according to any preceding claim, wherein the absolute pupil diameter is established by reference to a look-up table.

33. A pupilometer according to any preceding claims, wherein said bright light source is a bright white light source.

34. Image processing software comprising computer program instructions for causing a computer to perform the algorithm steps set out in any of Claims 20 to 32.

35. A process for obtaining pupil image information comprising the steps of:

i) Illuminating a pupil with the illumination means of a pupilometer according to any of Claims 1 to 33; and

ii) Running image processing software according to Claim 34.

36. A hand-held pupilometer comprising image capturing means, illumination means, stimulation means, image processing software, a hand-grip, a display, and command means, wherein said illumination means generates and emits light of a first wave-length, and said stimulation means generates and emits light of a second wavelength, and wherein said illumination means, in use, shines light towards the eyeball, the user viewing an image of the eye displayed on the display means, the said image having been captured by said capture means and processed by said image processing software.

37. A pupilometer substantially as shown in, and as described with reference to, the drawings.

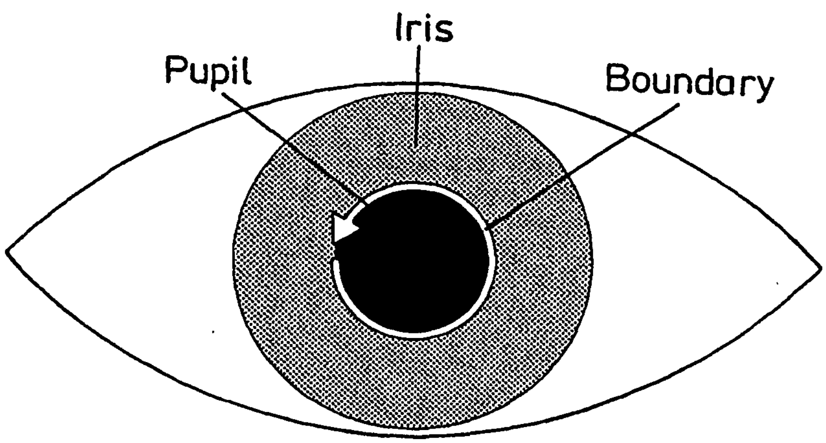


Fig. 1

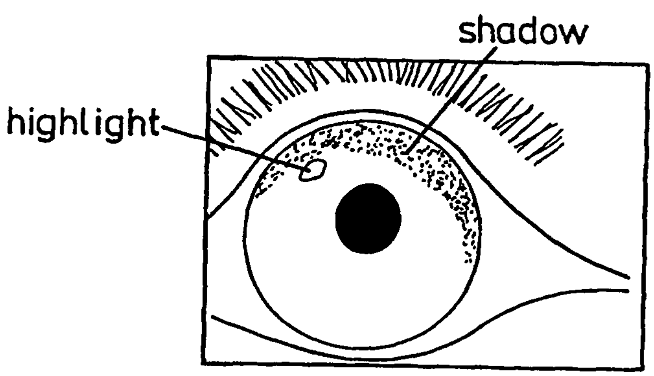


Fig. 4

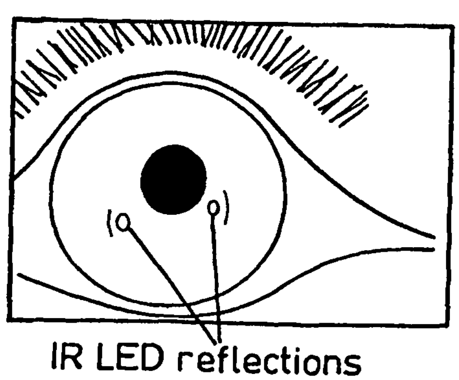


Fig. 5

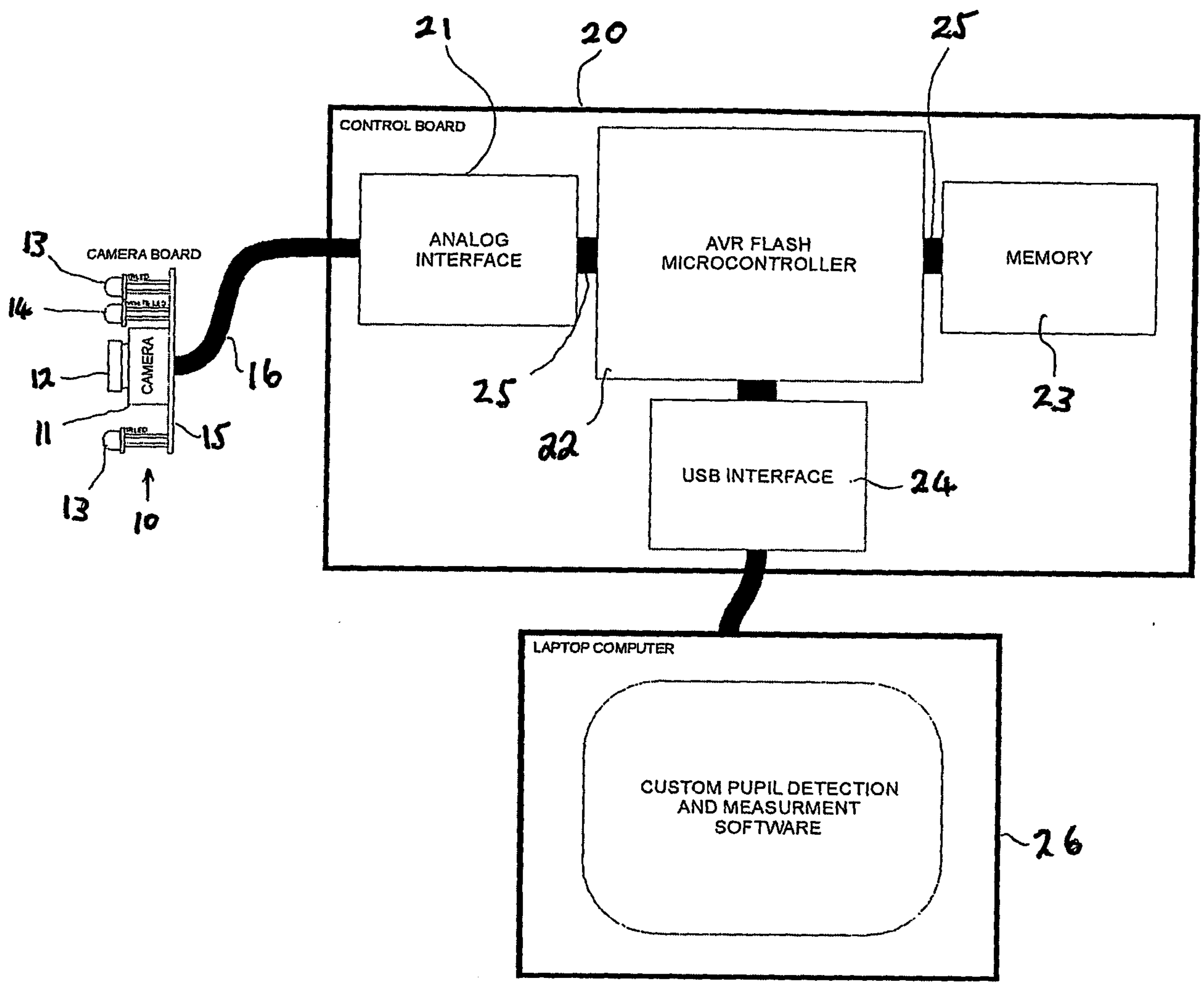

21
20
25
CONTROL BOARD
ANALOG INTERFACE
AVR FLASH MICROCONTROLLER
MEMORY
13
CAMERA BOARD
14
12
CAMERA
11
13
10
15
16
25
22
23
USB INTERFACE
24
LAPTOP COMPUTER
CUSTOM PUPIL DETECTION AND MEASURMENT SOFTWARE
26

Figure 2

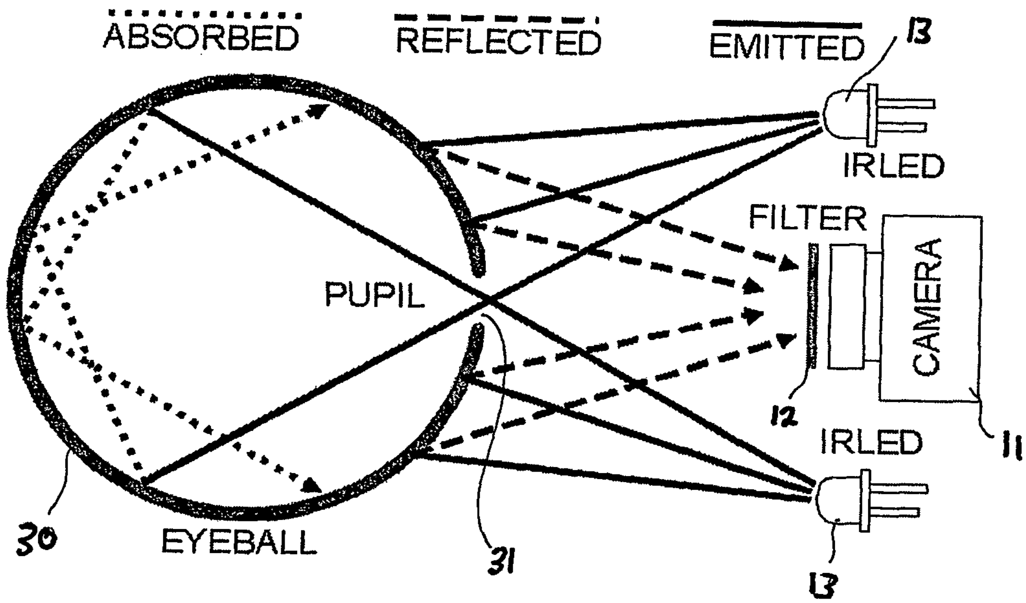

ABSORBED
REFLECTED
EMITTED
13
IRLED
FILTER
CAMERA
PUPIL
12
IRLED
11
30
EYEBALL
31
13

Figure 3

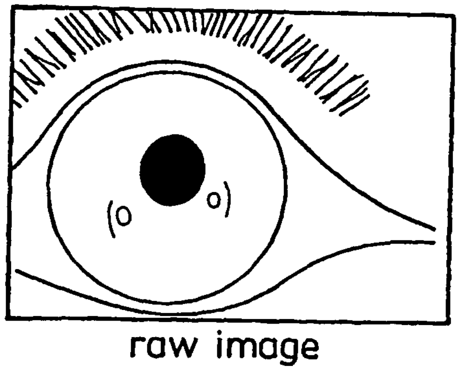


Fig. 6

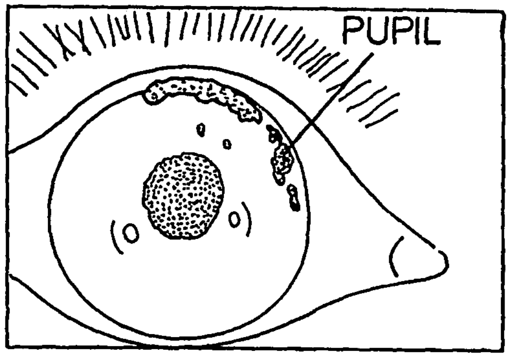


Fig. 7

P_0	P_1	P_2
P_3	P_4	P_5
P_6	P_7	P_8

Where G is the magnitude of the gradient across target pixel P_4

Fig. 8

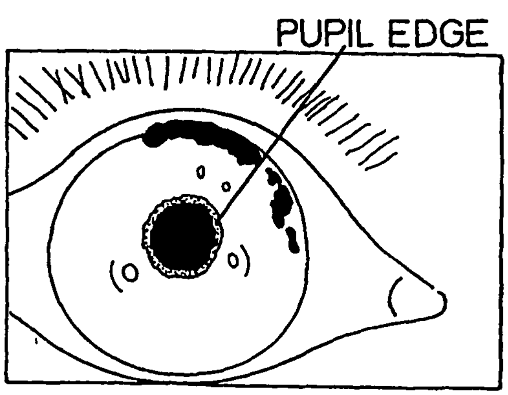


Fig. 9

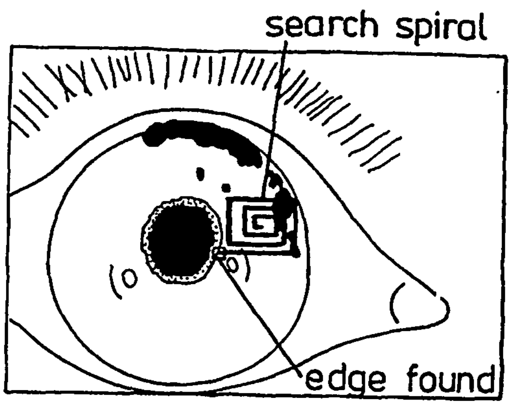


Fig. 10

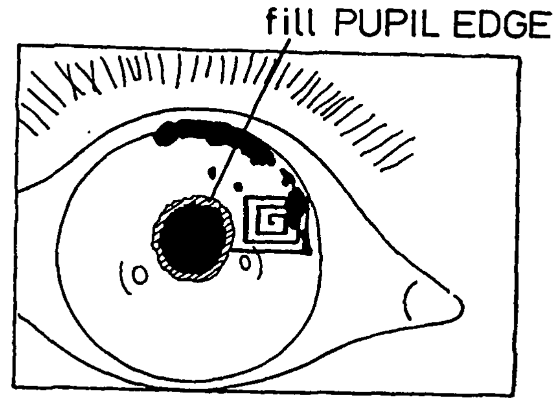


Fig. 11

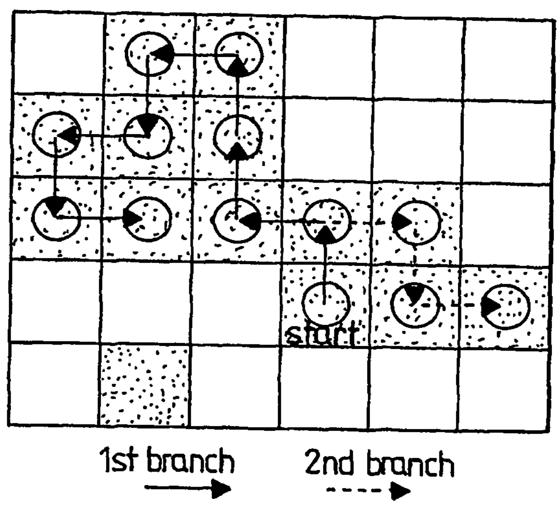


Fig. 12

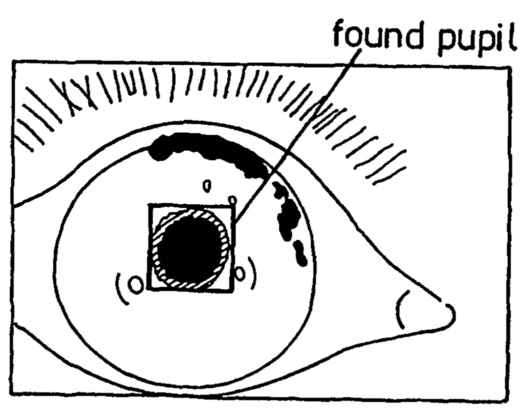


Fig. 13

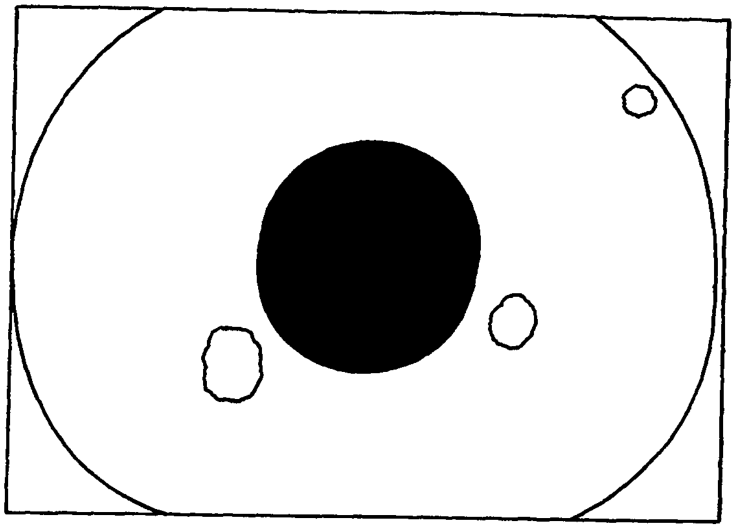


Fig. 14

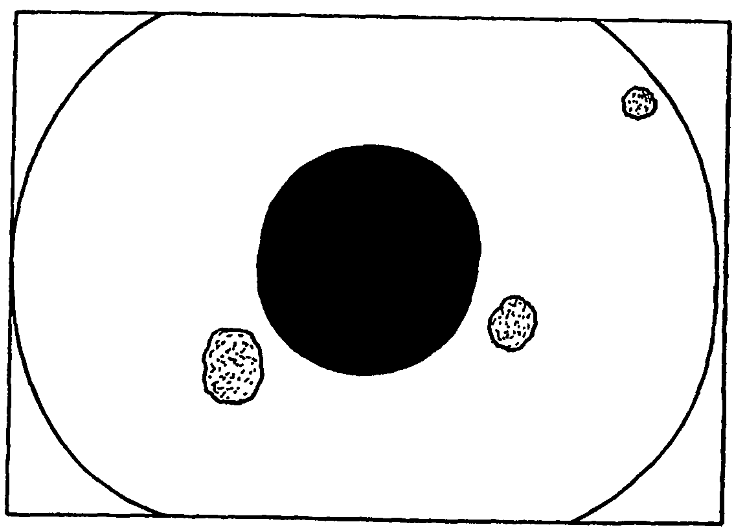


Fig. 15

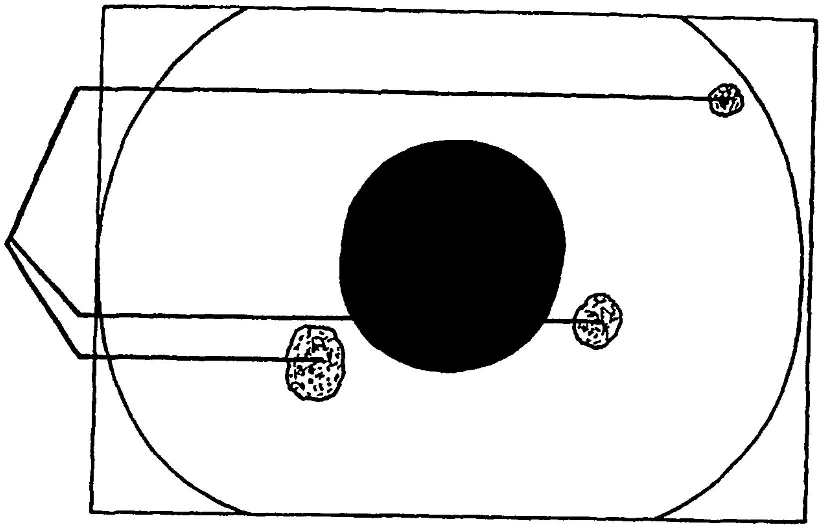


Fig. 16

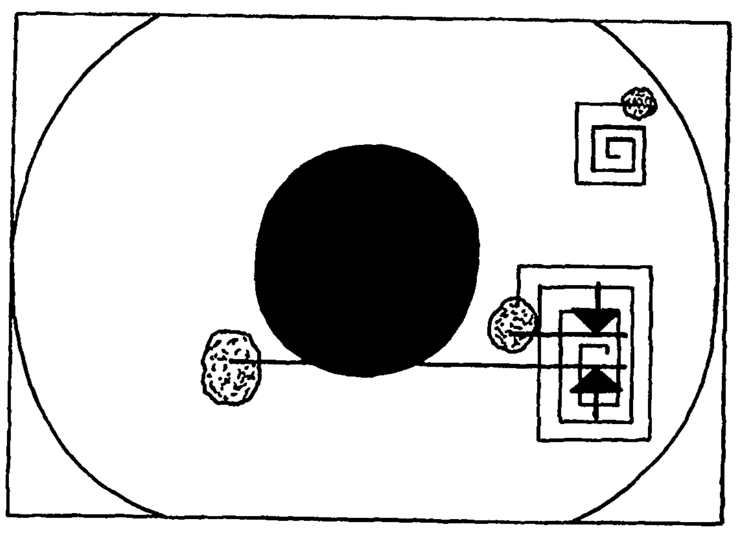


Fig. 17

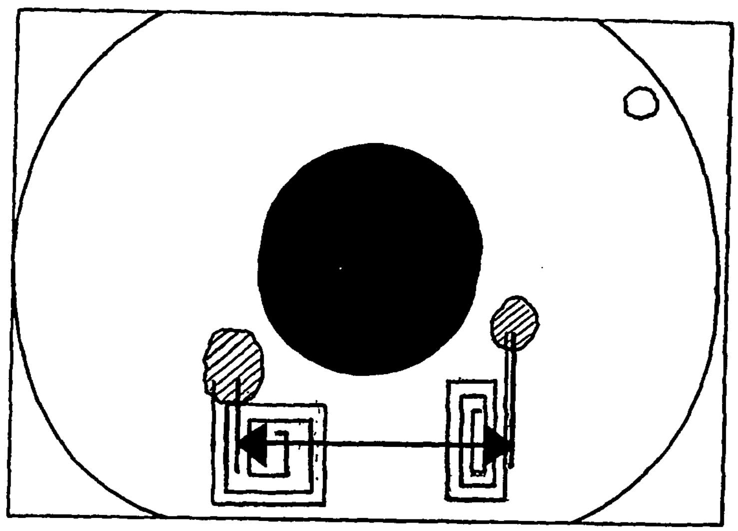


Fig. 18

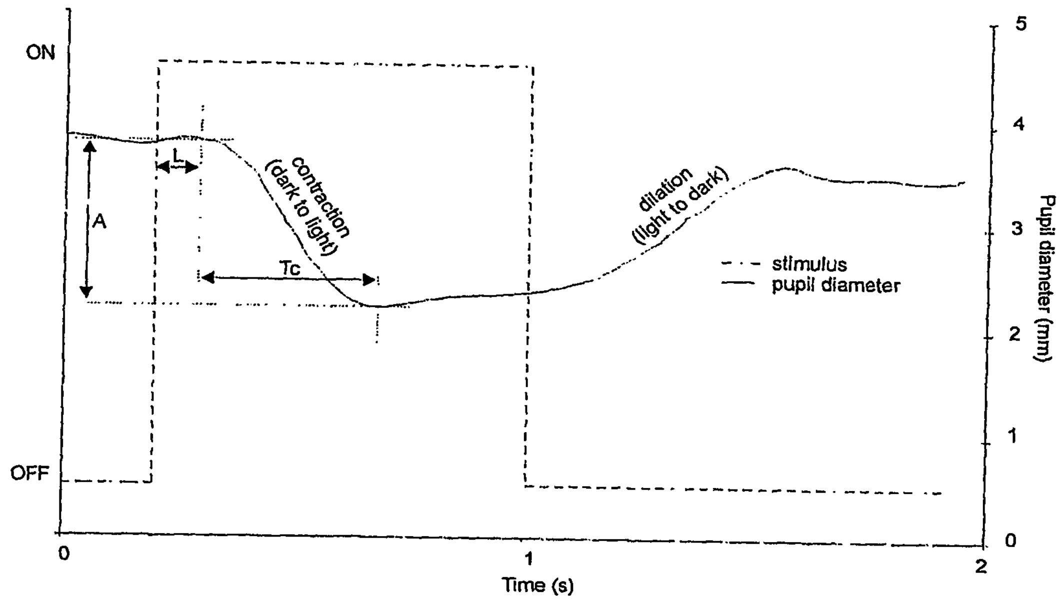
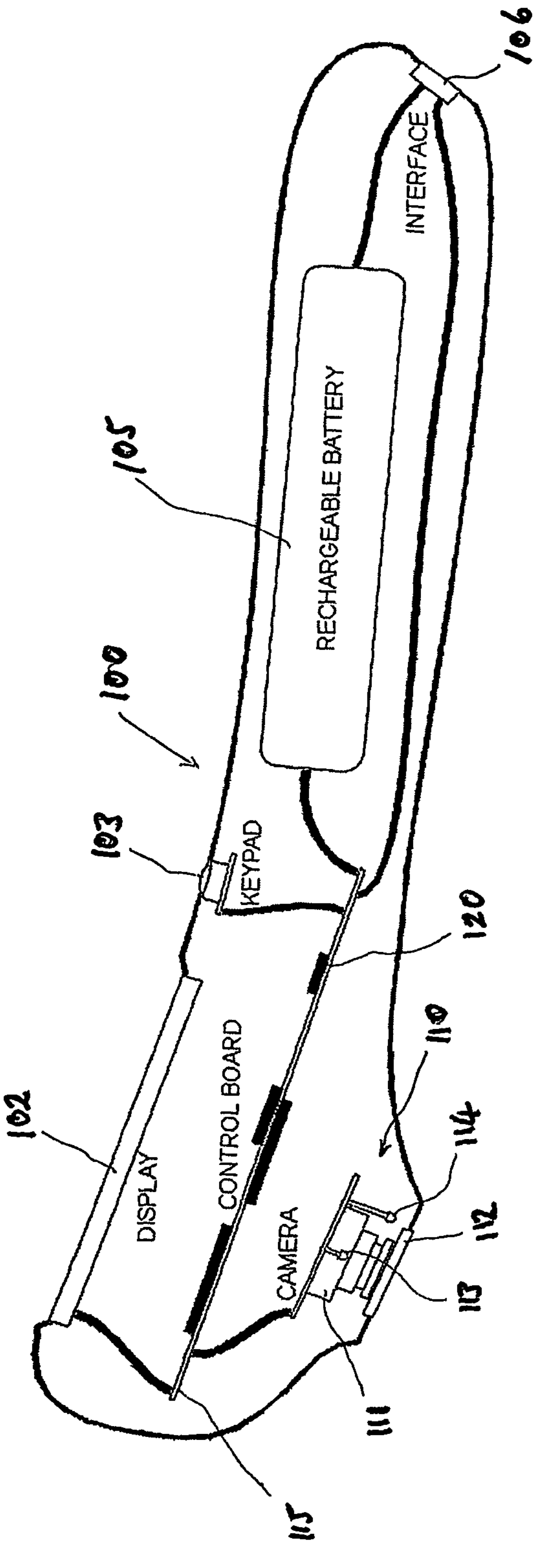

ON
OFF
A
L
Tc
contraction
(dark to light)
dilation
(light to dark)
stimulus
pupil diameter
0
1
2
Time (s)
0
1
2
3
4
5
Pupil diameter (mm)

Figure 19

Figure 20


106
INTERFACE
RECHARGEABLE BATTERY
105
100
103
KEYPAD
120
110
CONTROL BOARD
102
DISPLAY
114
CAMERA
112
113
111
115

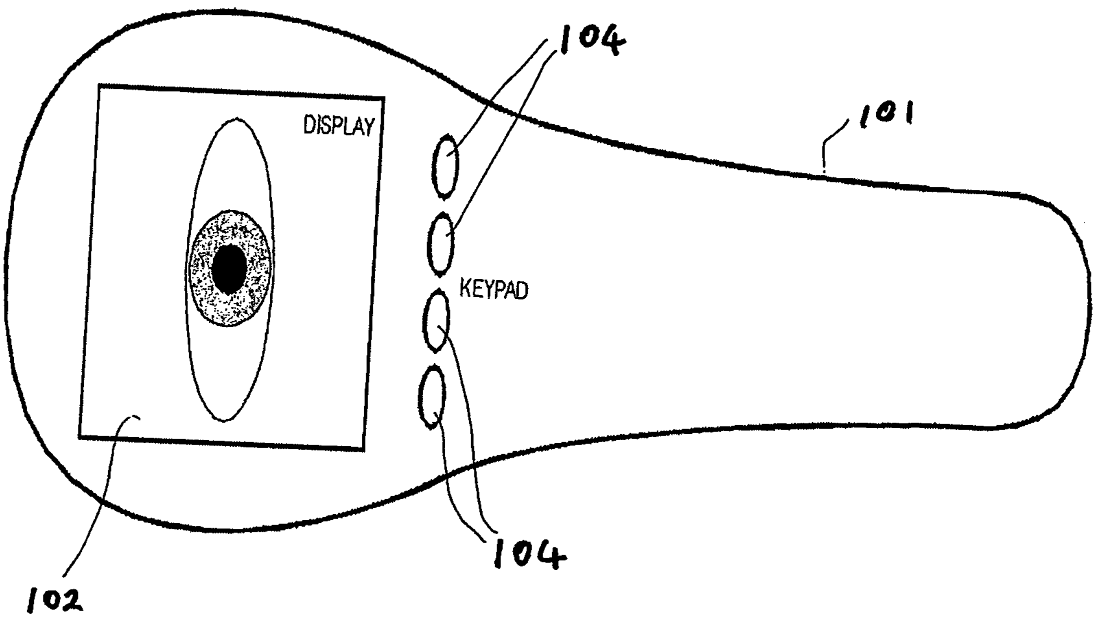
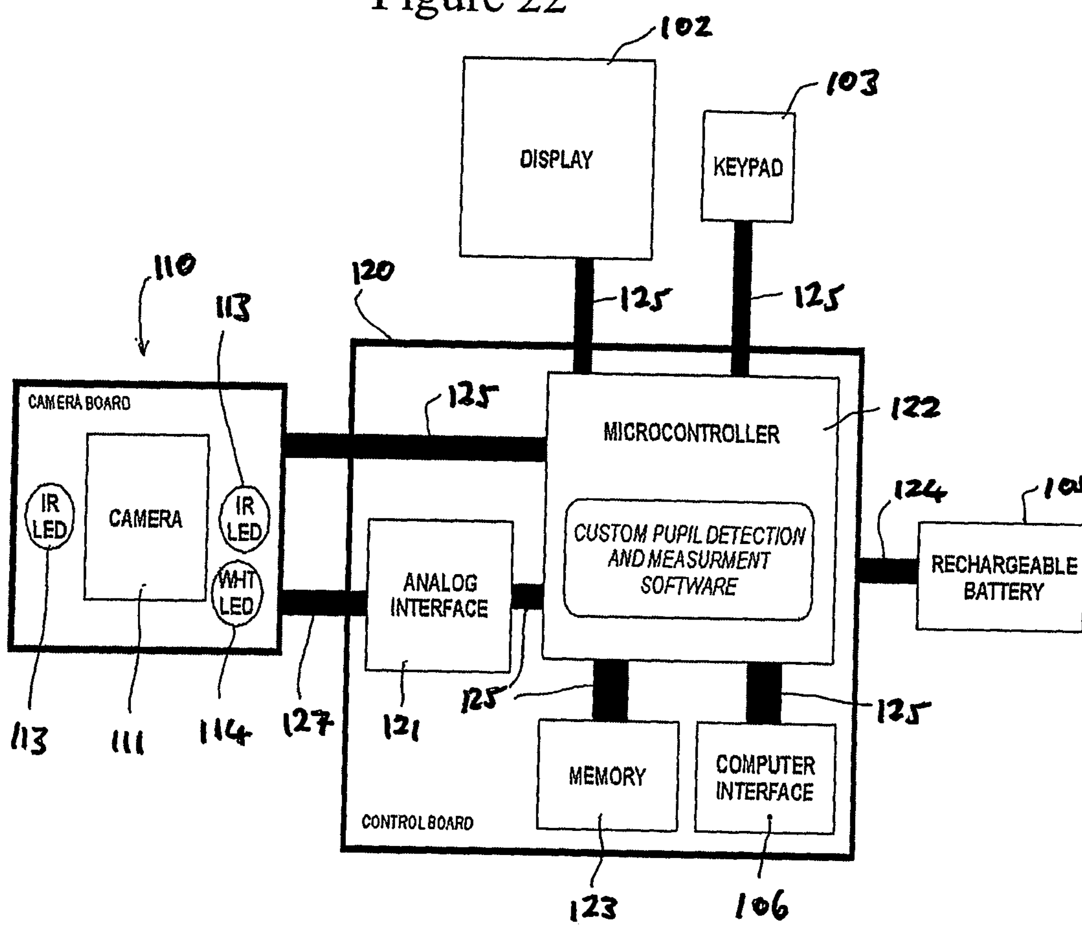


Figure 21

Figure 22


102
DISPLAY
103
KEYPAD
110
113
120
125
125
125
CAMERA BOARD
IR LED
CAMERA
IR LED
WHT LED
MICROCONTROLLER
122
CUSTOM PUPIL DETECTION AND MEASURMENT SOFTWARE
124
105
RECHARGEABLE BATTERY
ANALOG INTERFACE
125
125
113
111
114
127
121
MEMORY
COMPUTER INTERFACE
CONTROL BOARD
123
106

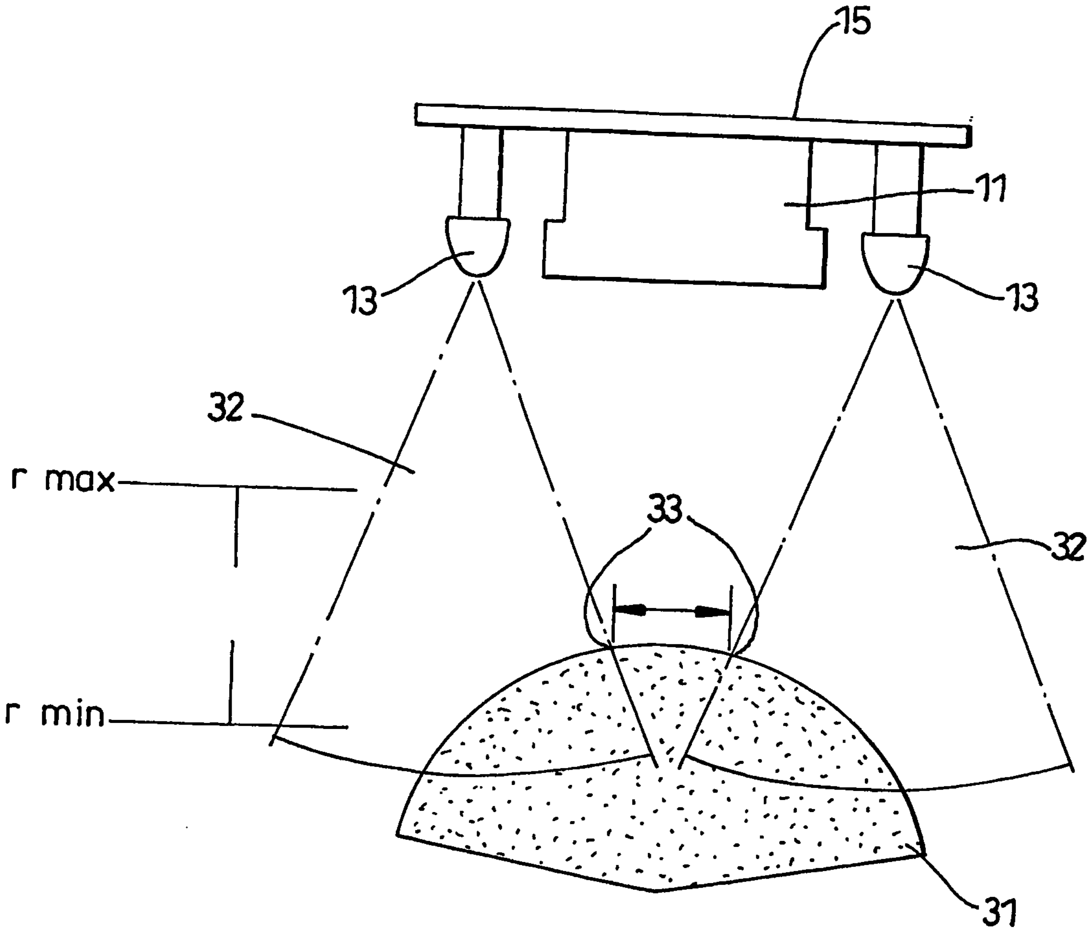


Fig. 23

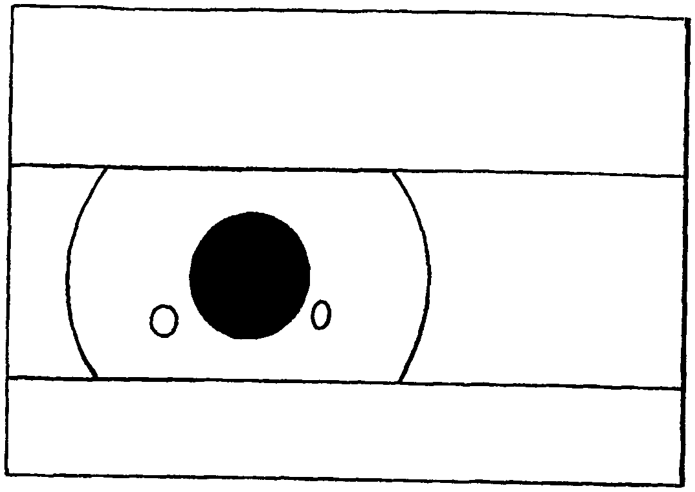


Fig. 24

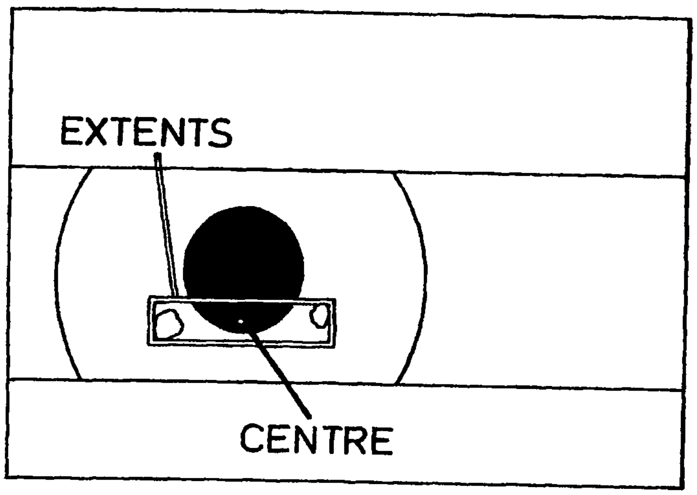


Fig. 25

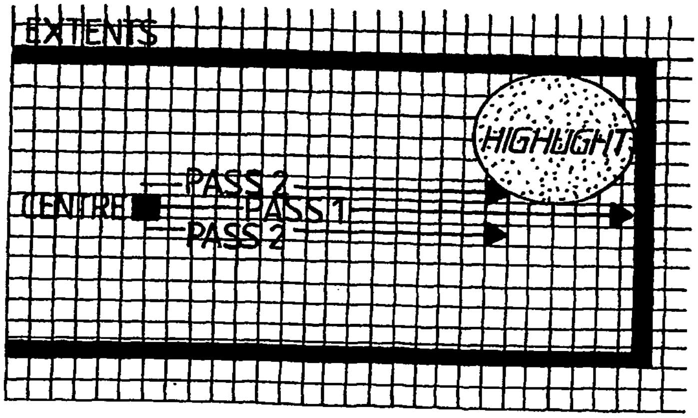


Fig. 26

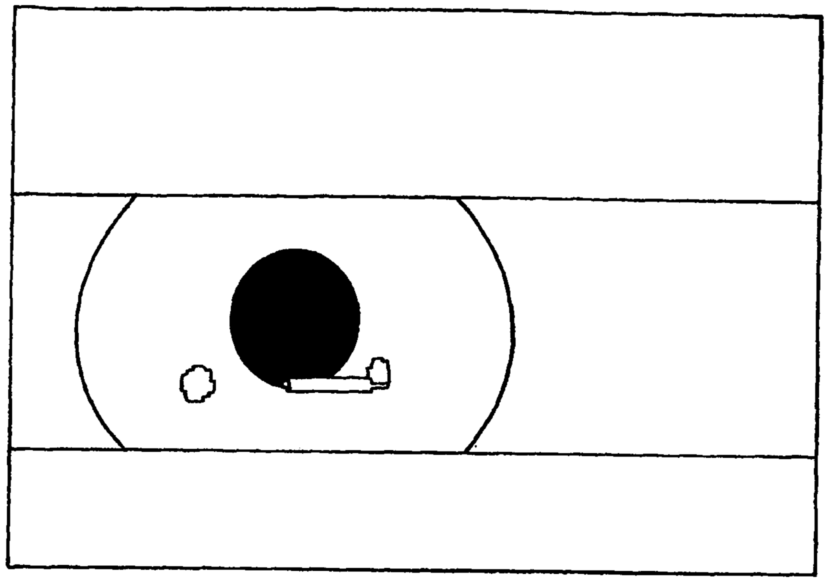


Fig. 27

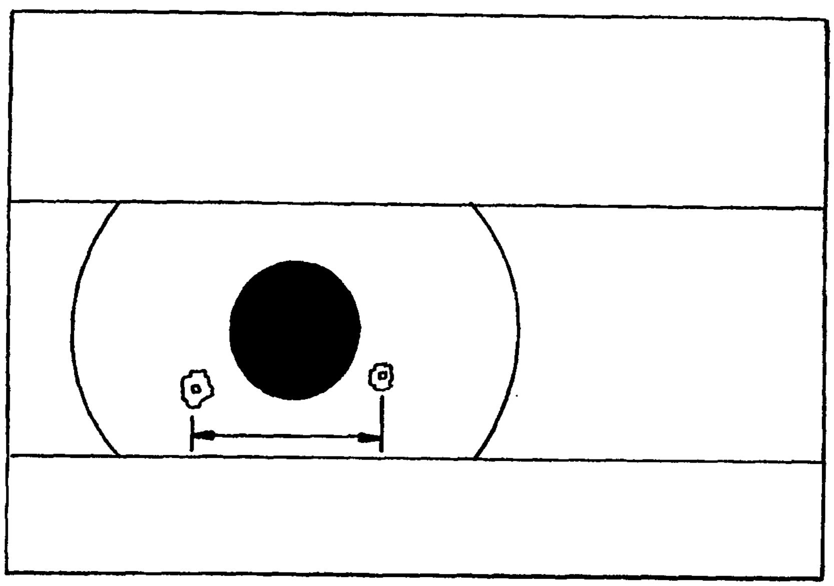


Fig. 28

INTERNATIONAL SEARCH REPORT

Application No
PCT/GB 03/05653

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61B3/11

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, INSPEC

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 260 968 B1 (PRIVITERA CLAUDIO M ET AL) 17 July 2001 (2001-07-17) cited in the application	36
A	column 3, line 51 -column 7, line 40	1-35

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
5 April 2004	15/04/2004

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Manschot, J

International application No.
PCT/GB 03/05653

INTERNATIONAL SEARCH REPORT

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☒ Claims Nos.: 37
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 37

Claim 37 defines the subject-matter by referring generally to the drawings and the description. This renders the claim unclear (Article 6 PCT) and is not allowed (Rule 6.2 PCT).

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Application No
PCT/GB 03/05653

Patent document cited in search report		Publication date	Patent family member(s)			Publication date
US 6260968	B1	17-07-2001	US	6116736	A	12-09-2000
			CA	2368232	A1	02-11-2000
			EP	1173089	A1	23-01-2002
			JP	2002541959	T	10-12-2002
			WO	0064330	A1	02-11-2000